CATGAAGGTTCCTCCTGTCCTGCTTCTCTTTCTTCTGTCCTCAGTGCGAGCTACTGAGCAACCGCAGGTCGTCACTG
AGCATCCCAGCATGGAGGCAGCCCTGACCGGGCCCAACGCCTCCTCGCACTTCTGGGCCAACTACACTTTCTCTGAC
TGGCAGAACTTCGTGGGCAGGAGACGTTATGGGGCCGAGTCCCAGAACCCCACGGTGAAAGCACTGCTCATCGTGGC
CTACTCATTCACCATCGTCTTCTCGCTCTTCGGTAATGTCCTGGTCTGTCATGTCATCTTCAAGAACCAGCGCATGC
ACTCGGCCACCAGCCTCTTCATTGTCAACCTGGCAGTGGCGGACATCATGATCACATTGCTCAACACGCCCTTCACT
TTGGTCCGCTTTGTGAACAGCACATGGGTGTTTGGGAAGGGCATGTGTCATGTCAGTCGCTTTGCTCAGTACTGTTC
TCTACATGTCTCAGCACTGACTCTGACAGCTATCGCAGTGGACCGCCACCAGGTCATCATGCATCCACTGAAGCCTC
GGATCTCCATCACCAAGGGTGTCATATATATTGCTGTCATCTGGGTCATGGCTACCTTCTTCTCTCTGCCACATGCC
ATCTGCCAGAAACTGTTTACCTTCAAGTACAGTGAGGACATTGTGCGCTCCCTCTGCCTGCCGGACTTCCCGGAGCC
AGCTGACCTCTTCTGGAAGTATCTGGACCTGGCCACCTTCATCCTGCTCTACCTACTTCCACTCTTCATTATCTCAG
TGGCCTATGCTCGTGTGGCCAAGAAGCTGTGGCTCTGTAACACCATTGGCGACGTGACCACAGAGCAGTACCTCGCC
CTGCGACGCAAGAAGAAGACCACCGTGAAGATGCTGGTGCTTGTGGTAGTCCTCTTTGCCCTCTGCTGGTTCCCTCT
CAACTGCTATGTCCTCCTCTTGTCCAGCAAGGCCATCCACACCAACAATGCCCTCTACTTTGCCTTCCACTGGTTTG
CCATGAGCAGTACTTGTTATAACCCCTTCATCTACTGCTGGCTCAATGAGAACTTTAGGGTTGAGCTTAAGGCATTG
CTGAGCATGTGCCAAAGGCCACCCAAGCCGCAGGAAGACAGGCTACCCTCCCCAGTTCCTTCCTTCAGGGTGGCATG
GACAGAGAAGAGCCATGGTCGGAGGGCTCCACTACCTAATCACCACTTGCCCTCTTCCCAGATCCAGTCTGGGAAGA
CAGATCTGTCATCTGTGGAACCCGTTGTGGCCATGAGTTAGGGAAAGCTGGAAGTTGGTGGGGGAGGGTTCTTTCCT
CTCACAATTGACCAGACACTAACAGAGTTGGAAAGTAACACAGAAGCAGTGAGATGCTTGGGTTCCTAGGAACCTGT
CCAGCCCCATCTGATTTGCAAACTTTCTAGAAGATGCCATGAGGTGGTGTGTGTAGATCTTTGAGCAAGAGCTCTGG
AAACCACCTCAGCTTCAACAGAGGCTGGTCCAGTCAACCACCTCCAATTGTGTAGCATCTGCCACCTTGCCCTTCCT
ACTGCTGAGCAACCACAGGGGGGACTTGAGCCATACTATTGGTGGGCCTGCCCCACATGCTCAGAAAAGAACAGGCAC
AAAGGCTTTCTGAAGTCATTGGAACAGGAATAATCACACAGCTTCAGTGACCTTGGCTCTATCCATGACCAGACAGG
ACCCATTTTGGCTTCTTAAAAACAAAGAGAAATTAGTATTGCCACTTTGAAAAGTTCAGAAAAGTAAAGAAATGAGT
TCAGCCCTCAATTTGTAAAAAAAGGAAAAAAGAAAAAAAAAGAAAAAGAAAGAAAAAAGCCTGTTAATATGCTGTA
AATTTATCTGTAGCTTTGCCTTCTGTGTGTGTACATTTGTACTTTTAAAATCCTGAACTACACGTGTCCATGTAGAT
TGTAATAATTAGCAAGAAACTGGAATATATCAGAGTATTATTGAATTC (SEQ ID NO:1)

MKVPPVLLLFLLSSVRATEQPQVVTEHPSMEAALTGPNASSHFWANYTFSDWQNFVGRRRYGAESQNPTVKALLIVA
YSFTIVFSLFGNVLVCHVIFKNQRMHSATSLFIVNLAVADIMITLLNTPFTLVRFVNSTWVFGKGMCHVSRFAQYCS
LHVSALTLTAIAVDRHQVIMHPLKPRISITKGVIYIAVIWVMATFFSLPHAICQKLFTFKYSEDIVRSLCLPDFPEP
ADLFWKYLDLATFILLYLLPLFIISVAYARVAKKLWLCNTIGDVTTEQYLALRRKKKTTVKMLVLVVVLFALCWFPL
NCYVLLLSSKAIHTNNALYFAFHWFAMSSTCYNPFIYCWLNENFRVELKALLSMCQRPPKPQEDRLPSPVPSFRVAW
TEKSHGRRAPLPNHHLPSSQIQSGKTDLSSVEPVVAMS (SEQ ID NO:2)

FIGURE 1

Underlined = deleted in targeting construct

Bold = sequence flanking Neo insert in targeting construct

GGGGTGGCAGTCGGCACCATCAGGCTCCCTTGGCGTTTCGGAGTTTTCTCTGTGGTCCCG
ACTCTCCGGAGGATCTCGGTTGTCTCCCAAGTCGGAACCTGGCACGGTCCAGGTTCACTC
GGAGGTCCGGGCTTCCTCTGTGCCCCGTGCCCCTCGCTCCCAGGCTCCCTCTGTGGTGTG
GACTCCTCTAGCCCGGTGCGCTCAGCCCCTCGCACCCAGCCTCCAGGCACAGAGCCCGGC
AGGGAGCTCAGCCCTTGTGCCTAGAGCTGCAGTGGCTGGACATGAAGGTTCCTCCTGTCC
TGCTTCTCTTTCTTCTGTCCTCAGTGCGAGCTACTGAGCAACCGCAGGTCGTCACTGAGC
ATCCCAGCATGGAGGCAGCCCTGACCGGGCCCAACGCCTCCTCGCACTTCTGGGCCAACT
ACACTTTCTCTGACTGGCAGAACTTCGTGGGCAGGAGACGTTATGGGGCCGAGTCCCAGA
ACCCCACGGTGAAAGCACTGCTCATCGTGGCCTACTCATTCACCATCGTCTTCTCGCTCT
TCGGTAATGTCCTGGTCTGTCATGTCATCTTCAAGAACCAGCGCATGCACTCGGCCACCA
GCCTCTTCATTGTCAACCTGGCAGTGGCGGACATCATGATCACATTGCTCAACACGCCCT
TCACTTTGGTCCGCTTTGTGAACAGCACATGGGTGTTTGGGAAGGGCATGTGTCATGTCA
GTCGCTTTGCTCAGTACTGTTCTCTACATGTCT**CAGCACTGACTCTGACAGCTATCGCAG**
TGGACCGCCACCAGGTCATCATGCATCCACTGAAGCCTCGGATCTCCATCACCAAGGGTG
TCATATATATTGCTGTCATCTGGGTCATGGCTACCTTCTTCTCTCTGCCACATGCCATCT
GCCAGAAACTGTTTACCTTCAAGTACAGTGAGGACATTGTGCGCTCCCTCTGCCTGCCGG
ACTTCCCGGAGCCAGCTGACCTCTTCTGGAAGTATCTGGACCTGGCCACCTTCATCCTGC
TCTACCTACTTCCACTCTTCATTATCTCAGTGGCCTATGCTCGTGTGTGGCCAAGAAGCTGT
GGCTCTGTAACACCATTGGCGACGTGACCACAGAGCAGTACCTCGCCCTGCGACGCAAGA
AGAAGACCACCGTGAAGATGCTGGTGCTTGTGGTAGTCCTCTTTGCCCTCTGCTGGTTCC
CTCTCAACTGCTATGTCCTCCTCTTGTCCAGCAAGGCCATCCACACCAACAATGCCCTCT
ACTTTGCCTTCCACTGGTTTGCCATGAGCAGTACTTGTTATAACCCCTTCATCTACTGCT
GGCTCAATGAGAACTTTAGGGTTGAGCTTAAGGCATTGCTGAGCATGTGCCAAAGGCCAC
CCAAGCCGCAGGAAGACAGGCTACCCTCCCCAGTTCCTTCCTTCAGGGTGGCATGGACAG
AGAAGAGCCATGGTCGGAGGGCTCCACTACCTAATCACCACTTGCCCTCTTCCCAGATCC
AGTCTGGGAAGACAGATCTGTCATCTGTGGAACCCGTTGTGGCCATGAGTTAGGGAAAGC
TGGAAGTTGGTGGGGGAGGGTTCTTTCCTCTCACAATTGACCAGACACTAACAGAGTTGG
AAAGTAACACAGAAGCAGTGAGATGCTTGGGTTCCTAGGAACCTGTCCAGCCCCATCTGA
TTTGCAAACTTTCTAGAAGATGCCATGAGGTGGTGTGTGTAGATCTTTGAGCAAGAGCTC
TGGAAACCACCTCAGCTTCAACAGAGGCTGGTCCAGTCAACCACCTCCAATTGTGTAGCA
TCTGCCACCTTGCCCTTCCTACTGCTGAGCAACCACAGGGGGACTTGAGCCATACTATTG
GTGGGCCTGCCCCACATGCTCAGAAAAGAACAGGCACAAAGGCTTTCTGAAGTCATTGGA
ACAGGAATAATCACACAGCTTCAGTGACCTTGGCTCTATCCATGACCAGACAGGACCCAT
TTTGGCTTCTTAAAAACAAAGAGAAATTAGTATTGCCACTTTGAAAAGTTCAGAAAAGTA
AAGAAATGAGTTCAGCCCTCAATTTGTAAAAAAAGGAAAAAAGAAAAAAAAAAGAAAAAG
AAAGAAAAAAGCCTGTTAATATGCTGTAAATTTATCTGTAGCTTTGCCTTCTGTGTGTGT
ACATTTGTACTTTTAAAATCCTGAACTACACGTGTCCATGTAGATTGTAATAATTAGCAA
GAAACTGGAATATATCAGAGTATTATTGAATTC
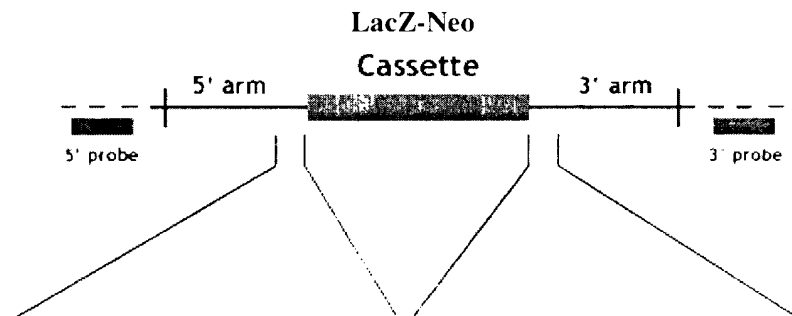
FIGURE 2A

Gene Sequence Structure *   299 bp   Sequence Deleted   753 bp

Size of partial
cDNA: 2253 bp

Targeting Vector*
(genomic sequence)

Construct Number: 463

Arm Length:
5': 2.5 kb
3': 0.6 kb

———— Targeting Vector
- - - - - Endogenous Locus

* Not drawn to scale

5'>CTGGCACGGTCCAGGTTCACT
CGGAGGCCCGGGCTTCCTCTGTGC
CCCGTGCCCCTCGCTCCCTGGCTC
CCTCTGTGGTGTGTGGACTCCTCTAG
CCCGGTGCGCTCAGCCCCTCGCAC
CCAGCCTCCAGGCACAGAGCCCGG
CAGGGAGCTCAGCCCTTGTGCCTA
GAGCTGCAGTGGCTGGACATGAAG
GTTTCTCCTGT<3'
(SEQ ID NO:3)

5'>CAGCACTGACTCTGACAGCTA
TCGCAGTGGACCGCCACCAGGTGA
GAGCACCTGTCCCCAGCAGCATGC
TCCCATCTCCGTCTATGCCTGGCT
GGCTGGTGGGAATACTGCCACCAC
GGTCTGTAGGGAATACTCTCAGGA
CAGTGACTCATTCAGTCCCGCTGA
CAGCGTGTGTGCTTGCCTCCTTGT
TGATCAATTTG<3'
(SEQ ID NO:4)

FIGURE 2B